



ANTIMICROBIAL POTENTIAL OF GINGER-ZINGIBER OFFICINALE

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ABSTRACT

Ginger [*Zingiber officinale*] has been used since many years in the various disciplines of medicine to treat multiple ailments. It is used in various forms like ginger tea, paste, jam, candy, preserved slices as home remedies. Various types of ginger extracts like cold or hot water extract, ethanolic, methanolic, hexanic or chloroform extract, soyabean oil extract or in the form of essential oil are used to study its properties. Ginger possesses anti-inflammatory, antioxidant, antimicrobial, antiangiogenesis, antineoplastic, hypolipidemic and antihyperglycemic properties. Its antimicrobial potential has been studied by many researchers and found that ginger exhibited antimicrobial property more against Gram positive than Gram negative organisms possibly due to the difference in their cell wall structure. Ginger also inhibited the growth of mycobacterium tuberculosis bacilli. Growth of human respiratory syncytial virus was inhibited by the ginger. It was also observed that ginger inhibited the growth of commonly observed fungal infections like candida albicans and aspergillus niger. Various studies revealed antiparasitic and anthelmintic actions of ginger. It has promising activity against *Trichomonas vaginalis* and *Toxoplasma gondi* infections as the drugs used for the treatment of these infections like metronidazole or sulphonamides are contraindicated in pregnancy. Ginger does not carry any teratogenic potential. Extensive clinical studies involving various forms of ginger, if conducted will encourage its usage as supportive antimicrobial agent to treat infections which will help to overcome antimicrobial resistance.

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INTRODUCTION

Ginger [*Zingiber officinale*] is a perennial herb belonging to the family Zingiberaceae. The rhizome of this plant is rich in phenolic compounds like gingerol, paradol, shogaol, volatile sesquiterpenes like zingiberene and bisabolene. It also contains monoterpenoids like curcumene, citral etc. Ginger is used as an ayurvedic medicine since ancient times. It has been used to treat conditions like arthritis, cramps, pains, sore throat, fever, rheumatism, infections, diabetes mellitus and even dementia.¹ It has antimicrobial action hence it is used to treat various infections.² It is relatively inexpensive, easily available, well tolerated, without any serious adverse reactions. It is generally recognized as safe [GRAS] by the US FDA.³

In addition to the use of ginger as a flavouring spice, it has been used in ayurvedic, tibbe-e-unani, aromatherapy, allopathy and in household remedies. Ginger rhizome is used in various forms like ginger tea, fresh paste, preserved slices, dried powder, cookies, jam, syrup, soda, beer and capsules.⁴

Ginger is a popular spice used globally especially in most of the Asian countries.⁵ Chemical analysis of ginger shows that it contains more than 400 different compounds. The major constituents in ginger rhizomes are carbohydrates, lipids,

terpenes, and phenolic compounds.⁶ Terpene compounds of ginger constitute zingiberene, β -bisabolene, α -farnesene, β -sesquiphellandrene, and α -curcumene. Phenolic compounds include gingerol, paradols, and shogaol. These gingerols and shogaol are the major contents of ginger. It also contains amino acids, raw fiber, ash, protein, phytosterols, vitamins like nicotinic acid and vitamin A and minerals.^{7,8} The aromatic constituents include zingiberene and bisabolene. The pungent constituents are gingerols and shogaols.⁹ Other gingerol or shogaol related compounds in ginger rhizome, are 6-paradol, 1-dehydrogingerdione, 6- gingerdione and 10-gingerdione, 4-gingerdiol, 6-gingerdiol, 8- gingerdiol, and 10-gingerdiol, and diarylheptanoids.^{1,10} Volatile oils like shogaols and gingerols impart the characteristic flavor and odor to the ginger.¹¹

Ginger is the most commonly consumed condiment worldwide. Ginger extract was found to possess wide range of activities like antibacterial, antifungal, analgesic, anticonvulsant, anticholinergic, antispasmodic, gastric antisecretory, antiulcer, antithrombotic, hypolipidemic, antihyperglycemic, antiallergic and antiserotonergic. It was also found to have antigenotoxic, anticarcinogenic, antimutagenic, anti-inflammatory and antioxidant properties both in vivo and in vitro studies.¹²

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Anti inflammatory activity of ginger

Infection invariably progresses to the inflammation involving various cytokines and chemokines. This enhances the oxidative stress on the tissue. Ginger was found inhibit the synthesis of the proinflammatory cytokines like tumor necrosis factor alpha [TNF alpha] and interleukin [IL] 1 and 8.¹³⁻¹⁵ The elevated expression of TNF alpha in rat liver cancer was blocked by ginger extract.¹⁶ Inflammation was found to be reduced by ginger through the inhibition of cyclooxygenase and 5-lipoxygenase pathways of arachidonic acid metabolism.¹⁷ Ginger also downregulated the activation of inflammatory genes.^{1,18} Inhibition of the synthesis of transcription factor like nuclear factor kappa B [Nf-kB] and the downregulation of expression of its genes were seen with the various constituents of ginger. This resulted in to the inhibition of cell proliferation and angiogenesis.¹⁹⁻²² Liposaccharide induced elevation in the levels of interferon gamma and IL-6 were suppressed by the ginger in the inflammatory tissue.²³

Antioxidant and free radical scavenging activity of ginger

Infections burden the inflammatory tissue with oxidative stress resulting in to the generation of reactive oxygen species [ROS].^{24,25} Ginger is a rich source of various antioxidant constituents which play a role in reducing lipid peroxidation and neutralizing ROS. It also scavenges superoxide and hydroxyl radicals.^{26,27} Gingerol was found to inhibit lipid peroxidation in rat liver microsomes.²⁸ Activated macrophages enhance the synthesis of nitric oxide in the process of inflammation which was observed to be reduced by the constituents of ginger like 6-shogaol, 6-dehydroshogaol and 1-dehydro-6-gingerdione.²⁹ Unsaturated ketone moiety of 6-shogaol was found to be responsible for its antioxidant property.³⁰ Phenolic constituents of ginger which were found to possess antioxidant property, scavenged H₂O₂ and after donating electrons to it converted in to the water.³¹

Antimicrobial activity of ginger

Antimicrobial property of plant preparation is believed to be due to tannins, saponins, phenolic compounds, essential oils and flavonoids.³² Ginger acts as an antimicrobial agent by preventing the growth of organisms. Researchers have prepared various extracts of ginger to study its antimicrobial potential. Ginger extract was prepared in various forms like cold or hot water extract, ethanolic, methanolic, hexanic or chloroform extract, soyabean oil extract or in the form of essential oil. Ethanol extract of ginger exhibited antimicrobial activity against *Salmonella typhi*, *Escherichia coli* and *Bacillus subtilis*.³³ Shagalol and gingerol were the active constituents of ginger responsible for its antibacterial and antifungal effect.³⁴ Ethanol extract of dry ginger powder significantly exhibited antifungal activity against *Candida albicans*.³⁵⁻³⁷ Gingerol the active constituent of ginger extract also showed antifungal action.³⁸ Ginger was also tried to treat periodontal infection induced by bacteria like *Staphylococcus aureus* and *Enterococcus faecalis*. They were inhibited by the active constituents of ginger like 6-gingerol and 12-gingerol.³⁹ In vitro studies showed, the antitubercular activity of 10-gingerol against *Mycobacterium tuberculosis* and *Mycobacterium avium*.⁴⁰

Ethanolic extract of dry ginger showed marked antibacterial activity against *Staphylococcus aureus* and *Enterococcus faecalis*, which form biofilms of microcolonies of these bacteria in periodontal infection. Though ethanol, on its own has an

antimicrobial property but this possibility was eliminated as ethanol got completely evaporated while preparing the extract, after heating it for 24 hours at temperature of 40 degree Celsius.⁴¹

Kamrul Islam *et al* studied the antimicrobial activity of soyabean oil extract of dry ginger powder. This exhibited in vitro antimicrobial activity against food borne pathogens like *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Vibrio cholerae*, *Klebsiella* and *Salmonella* species. Though the extract of ginger in soyabean oil was prepared at high temperature it could retain the antimicrobial activity of ginger.⁴² But Pankaj *et al* observed that ginger extract lost its antibacterial activity at boiling temperature.⁴³

Mohammed Nader *et al* observed that ethanol extract of ginger exhibited broader antibacterial activity than the essential oil. Cold water extract was more effective than hot water extract. Ethanolic extract had superior antimicrobial activity than antibiotics like ciprofloxacin, cephalixin, cephaloridin. It was more effective on gram positive than gram negative bacteria which may be related to the difference in their cell wall structure.⁴⁴ It is possible that ethanol being an organic solvent dissolves organic compounds better and liberates active compounds like gingerol, zingerone and shogaol which possess antimicrobial activity.⁴⁵

Ponmurgan karuppiah *et al* observed that ethanolic extract of ginger was found to be effective against gram negative organisms like *E. coli*, *P. aerogenosa*, *Klebsiella*, *Enterococci* and *Bacillus* species, who were resistant to almost 14 antibiotics.⁴⁶

Doaa Yassen studied the antimicrobial property of various types of ginger extracts. They observed that ethanolic, methanolic and hexanic extracts of ginger had profound inhibitory activity against *E. coli* and *Staph. aureus*. Chloroform extract inhibited growth of *S. aureus* without any effect on *E. coli*. Aqueous and acetic extract did not have any inhibitory activity against micro organisms studied. The solvent of extraction and its methods affect antimicrobial activity of ginger.⁴⁷ Antimicrobial activity of cold water extract of ginger was better than hot water extract as heat inactivates or destroys the antimicrobial active compounds of ginger like phenolic compounds.^{45,48}

Ginger is an ingredient of Ge-Gen-Tang [GGT]. GGT has been proved to have antiviral activity against human respiratory syncytial virus [HRSV]. GGT is a classic Chinese herbal formula invented 1800 years ago for the common cold. Recently it has been also used for cluster headaches. Sesquiterpenes [B-sesquiphellandrene] from fresh ginger was found to have anti viral effect against HRSV in human respiratory tract cell lines in dose dependent manner. Fresh ginger prevented the viral attachment and internalization of HRSV. High concentration of fresh ginger stimulated cellular secretion of interferon beta which contributed to counteract viral infection.⁴⁹ Denyer *et al* in 1994 reported anti HRSV and anti Rhinoviral activity of ginger.⁵⁰

Humayun Riaz *et al* found the inhibition of the growth of the fungi like *Candida albicans* and *Aspergillus niger* along with the inhibition of bacteria like *Staph. aureus*, *E. coli*, *B. subtilis* and *Streptococcus faecalis*.⁴

Okiki *et al* observed that the aqueous and methanolic extract of ginger has antimicrobial activity against seventeen gram

positive and gram negative bacterial species who were already resistant to antibiotics like cloxacillin, amoxicillin, erythromycin, streptomycin and cotrimaxazole in various degree. In this study the methanolic extract of ginger was found to be more effective than the aqueous, in inhibiting bacterial growth.⁵¹

Between the hexanic and methanolic extract of ginger, the hexanic extract of ginger was found to be less effective than the methanolic, against the tested gram positive bacteria like *Staph. aureus*, *Staph. epidermidis*, gram negative bacteria like *E. coli*, *Klebsiella*, *Proteus* and *Enterococcus* species and fungus like *Candida albicans*.⁵²

Ginger essential oil is characterized by high percentages of sesquiterpene hydrocarbons, mainly zingiberene, ar-curcumene, β -bisabolene, β -sesquiphellandrene, δ -cadinene and β -eudesmol.⁵³⁻⁵⁵ In addition monoterpenes camphene, geranial, geranyl acetate, linalool, 1,8-cineole and nerol have been reported as major components.^{53,56,57} The essential oil possesses antioxidant,⁵⁸ anti-inflammatory⁵³ and antimicrobial activities.^{53,55,58,59} This antimicrobial effect is well documented which is beneficial to treat the rising incidence of bacterial infections and to overcome antimicrobial resistance.

Antibacterial effect of ginger oil showed significant differences in the inhibition of Gram-positive and Gram-negative bacteria. Gram positive strains were more susceptible, suggesting that one of microbial targets of ginger oil is the bacterial cell wall, since Gram positive bacteria have a cell wall composed of a thick layer of peptidoglycan surrounding the cytoplasmic membrane, as against this gram negative bacteria have cell wall rich in lipopolysaccharides which is sandwiched between the outer and inner cell membrane.⁶⁰ However, it may have other microbial targets, such as plasma membrane, which explains its inhibitory effect on Gram negative bacteria, as the constituents of essential oils have been reported to have lipophilic properties which interact with the membranes, by altering their fluidity and permeability.⁶¹ Antimicrobial activity of spices like ginger is possibly due to the impairment of variety of enzymes which play role in generation of energy or synthesis of structural components of microbial cells.⁶²

Z. officinale was found to have a significant antihelmintic activity against *Schistosoma mansoni*, *Toxocara canis*, *Dirofilaria immitis*, *Angiostrongylus cantonensis*, *Anisakis simplex*, *Hymenolepis nana* and hydatid cysts either in vitro or in vivo. Also, it has an anti-protozoal effect against *Toxoplasma gondii*, *Giardia lamblia*, *Trypanosoma brucei* and *Blastocystis* species. It was also found to have insecticidal, molluscicidal and anti-leech effects.⁶³

Toxoplasma gondii [T.gondii], a parasitic infection affects central nervous system in immunocompromised patients. It is also responsible for repeated abortions. Ginger root extract [GE] and fraction 1 obtained from GE [GE/F1] was found to inhibit the expression of caspase-3, bax, p53 and p21 related to apoptosis causing the death of infected host cell. GE/F1 had direct anti T. gondii effect through the inhibition of the apoptotic proteins in the infected host cell. Suppression of the inflammatory cytokines secretion also contributes for this effect.⁶⁴

Ethanol extract of ginger was found to induce programmed cell death in *Trichomonas vaginalis* [T.vaginalis] infection in vitro. It does not carry teratogenic effect like 5-nitroimidazoles

e.g. metronidazole. Hence it can be preferred for T.vaginalis infection in pregnancy. Constituents of ginger like gingerol, shogaols and hexahydro-curcumine have direct effect on vitality and viability of parasite. It affects the cytogenicity of the T.vaginalis which involves its cytoadhesion and immune evasion. Saponins in the ginger possess detergent property which affect the bi-lipid layer of the parasite and inhibits its cytoadherence. Saponins inhibit the proteolytic activity of cysteine proteinases of the parasite responsible for adherence, procurement of nutrition and virulence. Saponins also inhibit the release of proinflammatory cytokines.⁶⁵

These antimicrobial actions of ginger extracts and ginger oil against bacterial species, viruses, parasites and helminths become more effective with the contribution of their anti-inflammatory and antioxidant potentials.

Ginger is a rhizome of *Zingiber officinale* having pleiotropic actions and various potential uses. Antimicrobial property of ginger extracts have been studied against various bacterial species, viruses, parasites and helminths with promising results. Ginger is universally available and has been used since ancient times. It is inexpensive and does not carry any serious adverse reactions like existing antibiotics. Hence the antimicrobial property of ginger needs to be extensively studied through the elaborate clinical trials so that its regular use can be encouraged in various infectious disorders.

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